## REMARKS

The Examiner has rejected claims 1-13. With this response, Applicants have amended claims 1, and 4-13, have canceled claims 2 and 3 without prejudice, and have added new claims 14-26. Thus, claims 1, and 4-26 are currently pending and under consideration, and Applicants have addressed the Examiner's rejections and objections in reference to the currently pending claims. Applicants respectfully submit that no new matter is presented with these amendments or additions.

*I. Objection to claims 1, 2, and 4-13:*

The Examiner has made an objection to claims 1, 2, and 4-13 as containing non-elected subject matter. In response to the Examiner's objection, Applicants have amended claim 1 (and claims dependent thereon) so that compounds of formula I only contain compounds drawn to the elected invention (e.g., $A_1$-$A_4$ are C-$R_1$, C-$R_2$, C-$R_3$, C-$R_4$, respectively and W is N).

*II. Objection to the Title:*

In response to the Examiner's suggestion, the title has been amended to read:

3-OXIMINO INDOLES AS INHIBITORS OF c-JUN N-TERMINAL KINASES (JNK)

*III. Objection to the Abstract:*

In response to the Examiner's assertion that the abstract is too short and generic, Applicants have amended the Abstract to include Figure 1 and a description of the utility.

*IV. Defective Oath/Declaration:*

In response to the Examiner's assertion that the oath/declaration is defective because non-initialed and/or non-dated alterations have been made to inventor Wilke's address, Applicants are in the process of obtaining from inventor Wilke a newly signed declaration. Applicants are having difficulty contacting inventor Wilke for the appropriate signature (inventor Wilke no longer works at Vertex Pharmaceuticals, Inc.); however, as soon as a new declaration is obtained, Applicants will submit the declaration.

*V. Claim Rejections under 35 U.S.C. § 112, second paragraph*

a) The Examiner has rejected claims 1, 2, and 4-13 and states that line 21, page 127 of claim 1 would appear superfluous after restriction. In response to the Examiner's rejection,

Applicants have amended claim 1 (and claims dependent thereon) to exclude any non-elected subject matter and respectfully request that the Examiner withdraw the rejection of claims 1, 2, and 4-13.

b) The Examiner has rejected claim 3 because of an improper reference to Table 1. In order to expedite prosecution Applicants have canceled claim 3, and thus Applicants respectfully request that the Examiner withdraw the rejection of claim 3.

c) The Examiner has rejected claims 5-13 and states that the claim does not set forth any steps involved in the method/process. In response to the Examiner's rejection, Applicants have amended claims 5-13 to recite the specific step of administering the composition of claim 4 to a patient. Applicants respectfully submit that this amendment is sufficient to overcome the rejection under 35 U.S.C. § 112 second paragraph and 35 U.S.C. § 101 and respectfully request that the Examiner withdraw both of these rejections.

*VI. Claim Rejections under 35 U.S.C. § 112, first paragraph*

a) The Examiner has rejected claims 5-13 and states that while the specification is enabling for Parkinson's disease, it does not provide enablement for preventing any diseases. In an effort to expedite prosecution, Applicants have amended claims 5-13 to exclude any reference to preventing diseases and thus respectfully request that the rejection of claims 5-13 be withdrawn.

b) The Examiner has also rejected claims 5-13 and states that the specification, while being enabling for treating Parkinson's disease, does not reasonably provide enablement for treating the multitude of diseases embraced by the claims. Applicants respectfully disagree with the Examiner and respectfully submit that the Examiner has not established a *prima facie* case of nonenablement.

As detailed in the 35 U.S.C. § 112 first paragraph training manual, establishment of a *prima facie* case of nonenablement requires first that the Examiner construe the claims to ascertain the meaning of the claims, and also requires that the Examiner sets forth "a reasonable explanation as to why [he/she] believes that the scope of protection provided by [the] claim is not adequately enabled by the description of the invention provided in the specification" *In re Wright*, 999 F.2d 1557, 1562, 27 U.S.P.Q. 1510, 1513 (Fed. Cir. 1993). Furthermore, as stated in the MPEP Section 2164.04 "To object to a specification on the grounds that the disclosure is not enabling with respect to the scope of the claim sought to be patented, the examiner must provide evidence or technical reasoning substantiating those doubts."

Before addressing the rejection, Applicants would like to point out that, as stated in the

MPEP, "if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the Examiner has evidence that the model does not correlate." See MPEP § 2164.02. Additionally, only a "reasonable correlation" is required, and the test does not have to be "highly predictive" nor are compounds required to be in clinical trials as the Examiner suggests.

In response to the Examiner's rejection, Applicants respectfully disagree and respectfully submit that the Examiner has not provided a reasonable explanation as to why the scope of protection provided by the rejected claims is not adequately enabled. Specifically, Applicants have provided, in the background section of the specification, several references correlating JNK-3 with certain disease states, which disease states are specifically recited in the claims. Additionally, Applicants have provided several examples in the specification (see Table 1) of compounds that exhibit the ability to inhibit JNK-3 activity, and more generally have provided guidance in the specification for the synthesis of compounds and for testing their ability to inhibit JNK-3. As but one example, in the background section of the application, Applicants describe certain references that implicate JNK-3 in various neurodegenerative diseases (in addition to Parkinsons's and Alzheimer's, see pages 4 and 5).

Because the references cited in the background section of the present application and those known in the art suggest a correlation between the inhibition of JNK-3 protein kinase with the treatment of diseases as claimed, and because the Examiner has not provided evidence that there is no correlation between the inhibition of JNK-3 and the treatment of these diseases, particularly for neurodegenerative diseases, Applicants respectfully submit that claims 1 and 4-24 (as newly amended) are indeed enabled. Accordingly, applicants respectfully request that the Examiner withdraw the rejection of claims 1 and 4-14.

*VII. Claim Rejections under 35 U.S.C. §102*

a) The Examiner has rejected claims 1, 2, 4, 5 and 13 under 35 U.S.C. §102(a) as being anticipated by Gaeta (WO 99/65875) and points specifically to compound XI. Applicants respectfully disagree with the Examiner's rejection and submit that Gaeta is not a proper reference for a rejection under 35 U.S.C. § 102(a) which requires that the invention was "...patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent". Applicants respectfully submit that the publication date of WO99/65875 is December 23, 1999, while Applicants' effective filing date (date of invention) is April 23, 1999, the

date on which provisional application number 60/130,752 was filed. As clarified in the priority information added to the specification above, this application is a continuation of PCT International Application PCT/US00/10866 filed April 21, 2000, which PCT application also claims priority to US Provisional Application serial number 60/130,752 filed April 23, 1999. Applicants thus respectfully request that the Examiner withdraw the rejection of claims 1, 2, 4, 5, and 13 in view of Gaeta.

b) The Examiner has also rejected claim 1 under 35 U.S.C. §102(a) as being anticipated by Guerry (WO 96/16046) and Esaki (EP 685,463). As detailed above, claim 1 has been amended to include a proviso, which proviso excludes compounds disclosed by Guerry and Esaki. Applicants thus respectfully submit that claim 1, as amended, is not anticipated by Guerry or Esaki and thus respectfully request that the Examiner withdraw the rejection of claim 1.

## CONCLUSION

In view of the arguments and amendments presented above, Applicants believe that currently pending claims 1 and 4-26 are currently in condition for allowance. Applicants would like to thank the Examiner for careful review of this application.

If it is believed that a telephone call would expedite prosecution, the Examiner is invited to contact the undersigned at (617) 444-6536. It is believed that there are no fees associated with this amendment; however, if Applicants are mistaken, the Commissioner is authorized to charge any fees (or credit any overpayments) to Deposit Account Number: 50-0725, reference number VPI/99-01 CON US.

Respectfully submitted,

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